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**From:** Robert L. Bernstein, Reg. No. 46,020  
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**Subject:** U.S. Patent Application 10/552,426  
Entitled: TIE-2 Modulators and Methods of Use

**Attorney**  
**Docket No.:** EX04-019C-US

**Total number of pages including cover sheet:** 7

#### OFFICIAL DOCUMENTS:

The following documents are attached for the above-referenced patent application:

1) Fax Cover sheet	1 page.
2) Transmittal Form	1 page.
3) Response to Restriction Requirement	5 pages.
	Total 7 pages

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**TRANSMITTAL  
FORM**

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

-8-

Application Number	10/552,428
Filing Date	July 6, 2008
First Named Inventor	Mohamed Abdulkader IBRAHIM
Art Unit	4161
Examiner Name	Brian McDowell
Total Number of Pages in This Submission	EX04-019C-US

**ENCLOSURES (Check all that apply)**

<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance Communication to TC
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment/Reply	<input type="checkbox"/> Petition	<input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Power of Attorney, Revocation	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Change of Correspondence Address	<input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Terminal Disclaimer	
<input type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> Request for Refund	1) Response to Restriction Requirement (5 pages).
<input type="checkbox"/> Certified Copy of Priority Document(s)	<input type="checkbox"/> CD, Number of CD(s) _____	
<input type="checkbox"/> Reply to Missing Parts/Incomplete Application	<input type="checkbox"/> Landscape Table on CD	
<input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53		
<b>Remarks</b>		
Please note that this document and its attachment were transmitted via fax to the USPTO at: 571-273-8300.		

**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT**

Firm Name	Exelixis, Inc.		
Signature	<i>Robert L. Bernstein</i>		
Printed name	Robert L. Bernstein		
Date	July 2, 2008	Reg. No.	48,020

**CERTIFICATE OF TRANSMISSION/MAILING**

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature	<i>Laura A. Huntington</i>		
Typed or printed name	Laura A. Huntington	Date	July 2, 2008

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Attorney Docket No.: EX04-019C-US

USSN: 10/552,426

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

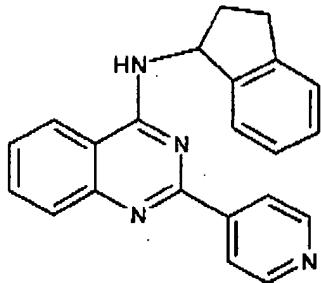
In the Application of: )  
 Mohamed Abdulkader IBRAHIM et al. )  
 USSN: 10/552,426 )  
 371 (c) Date: July 6, 2006 )  
 Confirmation No.: 6671 )  
 Examiner: Brian McDowell )  
 Group Art Unit: 4161 )  
 For: TIE-2 MODULATORS AND METHODS OF USE )  
 )

RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents  
 Post Office Box 1450  
 Alexandria, VA 22313-1450

In response to the restriction requirement issued on June 5, 2008, Applicants provisionally elect, with traverse, Group I, claims 1-32, drawn to compounds of general formula (I) stated in claim 1, wherein the heterocyclic ring containing Z form a quinazoline, and compositions thereof.

In view of this provisional election, Applicants elect the following species:



, which is compound #9 in Table 1.

The claims that read on this species are claims 1-9 and 30-32.

The Applicants traverse the restriction for the following reasons:

Claim 1 is generic. Accordingly, pursuant to MPEP §§ 803.02 and 809, the Applicants respectfully request the Office expand examination of the claims to the non-

elected portion of the generic claims, which, in the present instance, is the full scope of all claims.

As stated in MPEP § 809,

There are a number of situations which arise in which an application has claims to two or more properly divisible inventions, so that a requirement to restrict the claims of the application to one would be proper, but presented in the same case are one or more claims (generally called 'linking' claims) which, if allowable, would require rejoinder of the otherwise divisible inventions. See MPEP § 821.04 for information pertaining to rejoinder practice. . . . The most common types of linking claims which, if allowable, act to prevent restriction between inventions that can otherwise be shown to be divisible, are (A) genus claims linking species claims . . . . The linking claims must be examined with, and thus are considered part of, the invention elected. When all claims directed to the elected invention are allowable, should any linking claim be allowable, the restriction requirement must be withdrawn. Any claims(s) directed to the non-elected invention(s), previously withdrawn from consideration, which depends from or requires all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability.

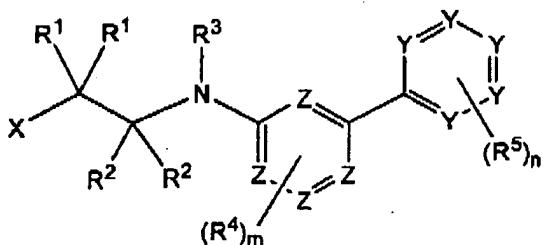
M.P.E.P. § 809 (emphasis added).

The applicants have the right to define what they regard as their invention, so long as their claims otherwise satisfy the statutory requirements. *In re Harnisch*, 206 U.S.P.Q. 300, 305 (C.C.P.A 1980). Applicants have the right to have each claim examined on the merits. *In re Weber et al.*, 198 U.S.P.Q. 328, 331 (C.C.P.A. 1978). Restriction of the subject matter of a single claim in a patent application is therefore generally impermissible because it denies the applicant the right to have that claim examined on the merits. *Id.* As the court stated in Weber, if "a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits." *Id.* Accordingly, "it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention." M.P.E.P. § 803.02.

The claims are written in Markush format. A Markush grouping is proper if the compounds in the Markush group share a single structural similarity and a community of properties (e.g., a common utility), such that the grouping is not repugnant to the principles of scientific classification. *Harnisch*, 206 U.S.P.Q. at 305; *Ex parte Brouard et al.*, 201 U.S.P.Q. 538, 540 (Bd. Pat. App. & Int. 1976). In other words, "unity of

invention exists where compounds share a common utility, and (2) share a substantial structural feature essential to that utility." M.P.E.P. § 803.02. The fact that the compounds in a Markush group may require different fields of search does not render the Markush group improper. *Brouard*, 201 U.S.P.Q. at 540. Also, where a Markush expression is applied only to a portion of a chemical compound, the propriety of the grouping is determined by consideration of the compound as a whole, and does not depend on there being a community of properties among the members of the Markush expression. *Id*; *Harnisch*, 206 U.S.P.Q. at 305; M.P.E.P. § 2173.05(h). In *Harnisch*, 206 U.S.P.Q. at 305, and as it is applied in *Ex parte Hozumi*, 3 U.S.P.Q.2d 1059 (Bd. Pat. App. & Int. 1984), the determinative factor for determining whether or not a Markush group is proper was held to be whether there existed "unity of invention," or rather whether the claims were drawn to a collection of unrelated inventions. Specifically, the claims in *Harnisch* were drawn to a class of substituted coumarin compounds disclosed as being "useful as dyestuffs." 206 U.S.P.Q. at 305. Accordingly, all of the claims had in common a functional utility related to a substantial structural feature disclosed as being essential to that utility.

Applicants submit that each of claims 1-38 possesses unity of invention. First, all of the compounds share a common utility as TIE-2 modulators. Second, each of the compounds in the Markush group share common structural features that contribute to their activity. Each of the compounds share the following significant structural features:



wherein the rings containing Z and Y are both aromatic moieties, and wherein the Z containing ring is attached to the substituted amine as shown above. Accordingly, all of the compounds read upon by the claims share common utility and structural features essential for that utility.

In view of the foregoing, the applicants submit that the claims are proper Markush claims and should be examined fully on their merits as generic linking claims for the elected group. To do otherwise would infringe on Applicants' "right to have each claim examined on the merits." *Weber*, 128 U.S.P.Q. at 331.

The proper procedure for examining Markush claims is provided in M.P.E.P. § 803.02:

A Markush-type claim may include independent and distinct inventions. ... In applications containing a Markush-type claim that encompasses at least two independent or distinct inventions, the examiner may require a provisional election of a single species prior to examination on the merits. ... Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable, the provisional election will be given effect and examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

\* \* \*

On the other hand, should the examiner determine that the elected species is allowable, the examination of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a *nonelected species*, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The examination will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action can be made final unless the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p).

Pursuant to MPEP 803.02 and 809, the entire scope of the claims must be examined.

No fees are believed to be due in order to process this document and any paper attached. Should the U.S. Patent Office determine that an extension of time and/or

other relief is required at this time, the Commissioner is authorized to charge the cost of such relief and/or fees to Deposit Account No. 50-1108, referencing EX04-019C-US.

Respectfully submitted,

Date: July 2, 2008

  
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